EAS-E Suite Phase 1 Proof of Concept: Integrating different dermal exposure models with tiered PBPK models

Jon Arnot, Alessandro Sangion, James Armitage, Trevor Brown, Liisa Toose. *ARC Arnot Research and Consulting*.
Li Li. *University of Nevada Reno*.

Quantifying chemical exposure by the dermal route is an important element of safety evaluations for product stewardship and regulatory decision making. In a number of recent TSCA risk evaluations, the approaches used in evaluating the dermal route of exposure for workers and consumers have indicated the need for improving the scientific basis of dermal exposure modeling. To address this need to improve dermal exposure modeling, this research project includes:

1. Coding selected dermal permeation and absorption models in the Exposure And Safety Estimation (EAS-E) Suite platform (https://arnotresearch.com/eas-e-suite/). The dermal models will include the dermal exposure modules in IH-SKINPERM, Consumer Exposure Model (CEM), SHEDS-HT, RAIDAR-ICE, PROTEX, and TRA
2. Coding a time-dependent version of a one-compartment PBTK model within EAS-E Suite that can predict blood and urine concentrations following dermal exposure
3. Integration of the aforementioned dermal absorption models within EAS-E suite with steady state and time-dependent PBTK models to enable both, or either, chronic (steady-state) and acute (event-driven) exposure scenarios. Include a user option to provide empirical estimates for dermal absorption in place of model predictions for dermal absorption
4. Integration of these models in EAS-E suite with model input parameter databases, i.e., physical chemical, QSARs and TK (in vitro, in vivo and in silico), to enable auto-parameterization of the modules
5. Investigation of the potential to expand the applicability domain of the models to include ionizable organic chemicals
6. Developing, in consultation with ACC LRI, criteria for use in selecting potential candidate substances to be used in case studies
7. Using the dermal models incorporated into the EAS-E suite platform, conduct case studies that compare dermal exposure models for worker and consumers, for both steady state and event driven exposure scenarios. To include comparing outcomes of different dermal exposure models and different exposure scenarios.

Implications: This research will enhance and expand capacity for predictions of human exposures using various dermal exposure models and exposure scenarios. Linking the dermal exposure modules with the PBTK models will build capacity for comparing dermal exposure estimates with biomonitoring data (consumer or occupational). This work will facilitate the application, evaluation and comparison of exposure tools used by multiple stakeholders to support for decision-making.

Key words: dermal exposure, exposure modelling, PBPK models, biomonitoring

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